Further Studies Concerning the Pathogenesis and Treatment of Peritonitis *

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IN A RECENT SURVEY of the records of patients with fulminating peritonitis treated at the University Hospital between 1955 and 1960, there were 20 deaths among 58 cases. This points out that there still exists an appreciable mortality from peritonitis despite the many advances in antimicrobial and replacement therapy. In a study of 235 unselected cases of peritonitis, Wright *et al.*[12] reported an over-all mortality rate of 9.36 per cent. Some of the patients in their series died from causes other than infections but a mortality rate of 3.18 per cent was considered to represent the number of patients who died from uncontrolled infection despite vigorous antibiotic therapy. Many experimental studies dealing with the treatment of peritonitis were carried out during the early part of the last decade. Since that time, however, there has been very little investigation in this field.

Because of the importance of this unsolved problem and because of the increasing incidence of severe gram-negative infections,[5] it seemed important to initiate further studies concerning the pathogenesis and treatment of peritonitis. Previous workers have produced experimental peritonitis by some type of intra-abdominal operation in which fecal contamination from the colon produced the disease.[9-14] Most reports show thorough and careful studies but the detailed experimental preparation apparently prevented the use of an adequate number of animals to produce statistically significant results. Since Barnett [2] had so successfully used a standardized solution of toxic fluid for the evaluation of various modalities of therapy in strangulation obstruction, it was believed that a standardized fecal suspension injected into the peritoneal cavity of a significant number of dogs would serve as an ideal preparation for the study and evaluation of various treatment regimens in peritonitis.

Materials and Methods

Preparation of the Standardized Fecal Suspension. Mongrel dogs were anesthetized, a colotomy was performed, and fecal material was obtained from the transverse and descending colon. This fecal material from several animals was pooled, diluted with saline and homogenized with a Waring blender. To remove some of the solid particulate matter the fecal suspension was filtered through one layer of cheesecloth. The preparation was standardized on a cubic centimeter per kilogram basis by its lethal effect after intraperitoneal injection into normal dogs. Three such standardized suspensions were made and

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are referred to in this report as Feces I, Feces II and Feces III.

Plan and Conduction of the Experiments. Each experiment evaluating a specific modality of treatment was carried out in the following fashion. A small group of control animals and a few animals of each experimental study group were observed at the same time. Thus, in each series of any particular experiment, some animals in each category were under observation at the same time, meaning that various treatment regimens were compared with each other and with the controls under the same identical conditions.

Statistical significance was computed by the use of the Chi square test for small numbers with the Yates correction.

Method of Injection. The challenging dose of fecal suspension was always given on a cubic centimeter per kilogram basis. Mongrel dogs of either sex were used varying in size from 5.0 to 20 kg. Most of the animals, however, were approximately 10 kg. All of the experiments were concluded at the end of 24 hours and survival rates were calculated at that time. Since the fecal suspensions were standardized so that about 1.0 cc./kg. of body weight would produce a mortality of at least 80 per cent in a 24-hour period, it was believed that determining survival at the end of 24 hours would compensate for any variability in the animals.

A 20 or 30 cc. syringe with a 13-gauge needle was used to inject the fecal suspension into the peritoneal cavity. The technic of injection consisted of stretching the dog on his back on the floor and holding him as stable as possible. The needle was inserted at a 45 degree angle (pointed slightly to the animal's right to avoid the spleen) through the upper abdominal wall into the peritoneal cavity just below the angle of the rib cage. Particular care was taken to avoid injection into the intra-abdominal viscera. During the many injections necessary for standardization of the fecal suspension sufficient experience was gained in the technic of injection by one operator that failure to place the dose of feces in the peritoneal cavity almost never occurred as evidenced by operative and postmortem observations.

Administration of Antibiotics. In each experiment the amount of fluid used for the suspension of the calculated dosage of antibiotics injected was approximately the same in all animals. Usually the antibiotic or combination of antibiotics was diluted in 15 to 20 cc. of saline for intraperitoneal injection. Penicillin G, kanamycin sulfate, streptomycin sulfate and chloramphenicol succinate were used.

Technic of Irrigation. The dog was given the challenging dose of fecal suspension. Later, according to the time in the protocol, he was placed under light intravenous Nembutal anesthesia and a 10 cm. midline incision was made. One liter of the irrigating solution was introduced through the incision into the peritoneal cavity. Care was taken to make sure that it washed the surfaces of the peritoneal contents. By compressing the abdominal cavity, the excess fluid was removed. The incision was closed in two layers with continuous cotton sutures. To prevent leakage the antibiotic solution was placed in the peritoneal cavity as the first layer of the closure was completed. Control dogs were handled in the same manner as the treated animals except lavage was not performed.

Hematocrit Determinations. Blood was removed from the femoral vein at hourly intervals. Microhematocrit determinations were made using heparinized tubes.

Bacterial Counts. An incision was made over the femoral vein and it was either catheterized or left exposed using aseptic technic. Blood samples were taken at hourly intervals and placed in cold heparinized tubes. The samples were then diluted and spread over the surface of Trypticase soy agar plates and incubated

TABLE 1. *Number of Aerobic Microorganisms per Milliliter Appearing in Bloodstream after Intraperitoneal Injection of 1.5 cc./kg. Fecal Suspension*

Hours after Injection	Dogs										
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11
Control	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG
1	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG
2	NG	NG	NG	NG	NG	3.3×10^{3}	NG	NG	NG	NG	NG
3	NG	7.2×10^{2}	3.0×10^{1}	NG	NG	1.4×10^{2}	1.1×10^{2}	NG	NG	NG	NG
4	4.0×10^{3}	—	6.0×10^{2}	NG	NG	3.3×10^{3}	—	NG	NG	3.0×10^{1}	NG
5	1.7×10^{2}	1.0×10^{4}	2.4×10^{3}	3.0×10^{1}	NG	—	3.5×10^{2}	NG	4.0×10^{1}	1.2×10^{2}	NG
6	3.5×10^{2}	5.6×10^{3}	4.0×10^{4}	2.4×10^{2}	NG	—	5.0×10^{2}	NG	3.0×10^{1}	3.5×10^{2}	NG
7	1.8×10^{3}	4.5×10^{4}	5.7×10^{4}	—	NG	4.0×10^{4}	Died	NG	3.0×10^{1}	1.6×10^{3}	NG
8	1.6×10^{4}	Died	Died	1.0×10^{2}	NG	Died	—	NG	6.0×10^{1}	Died	NG
9	1.9×10^{2}	—	—	1.6×10^{3}	NG	—	—	NG	1.0×10^{2}	—	Died
10	Sacrificed	—	—	Sacrificed	NG Died	—	—	NG Died	Sacrificed	—	—

aerobically for 48 hours at 37° C. No attempt was made to cultivate anaerobic micro-organisms in this study.

Results

Appearance of Micro-organisms in the Bloodstream after Intraperitoneal Injection of the Fecal Suspension. After control samples had been obtained from the femoral veins, a fecal suspension (1.5 cc./kg.) was injected intraperitoneally into 11 dogs. The animals received no treatment. Further samples of femoral blood were drawn at hourly intervals. The counts of the aerobic micro-organisms are shown in Table 1. In Animals 5, 8 and 11 no growth occurred in any of the samples despite the fact that all the dogs died. The explanation for this is not immediately apparent.

In the majority of the animals, however, bacteria were not detected in the bloodstream during the first two hours after injection. Micro-organisms began invading at the third hour and increased in number until the animal died, usually between the seventh and ninth hours. At this time there were up to 10^4 aerobic micro-organisms per milliliter present in the bloodstream. Thus, the bacteremia in this experimental preparation apparently developed between the second and third hours and increased in severity until death. This is graphically displayed in Figure 1.

Effect of Single Antibiotics and a Combination of Antibiotics on Experimental Peritonitis. Dogs were injected with 1.0 cc./kg. of Feces I intraperitoneally. Immediately thereafter, the treated animals were given antibiotics by the same route.

TABLE 2. *Effect of Antibiotics on Experimental Peritonitis*

Feces I (1 cc./kg.)—followed by immediate intraperitoneal antibiotics

Category	No. Dogs	No. Surviving	% Survival	P Value
Control	20	2	10	<0.01
Penicillin (1 million units)	20	11	55	
Kanamycin (0.5 Gm./kg.)	20	12	60	<0.01
Penicillin (1 million units) and kanamycin (0.5 Gm./kg.)	20	20	100	
	—			
	80			

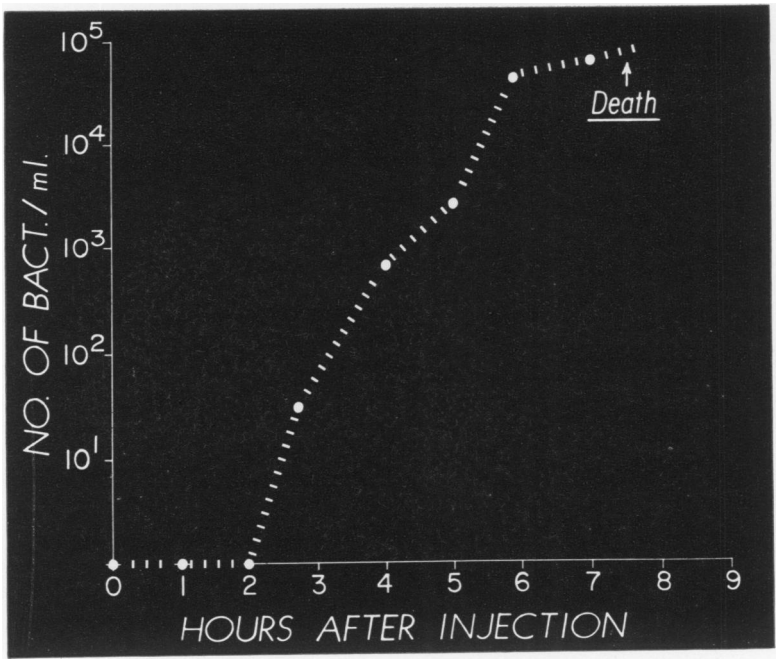

FIG. 1. Typical graph of number of microorganisms per milliliter in bloodstream at various times after intraperitoneal injection of a lethal dose of fecal suspension.

There were 20 dogs in each category. Comparison was made of a dose of 1 million units of pencillin, a dose of 0.5 Gm./kg. of kanamycin and a combination of the two (Table 2). Penicillin produced a 55 per cent survival which was significantly different from the 10 per cent survival in the control group. A combination of penicillin and kanamycin produced 100 per cent survival which was significantly different from the 60 per cent survival produced by the use of kanamycin alone. A significant increase in survival was seen with the use of all antibiotics in this experiment. The effect of 1 million units of penicillin and the large dose of 0.5 Gm./kg. of kanamycin was not significantly different. A combination of penicillin and kanamycin, however, was better than either antibiotic alone.

Comparison of the Effects of Various Antibiotic Combinations on Experimental Peritonitis. The oldest antibiotic combination for use in the clinical management of peritonitis is penicillin-streptomycin. Penicillin-kanamycin was chosen as one of the test combinations because of the broad spectrum and bactericidal effect of kanamycin. Barnett[2] has shown the efficacy of penicillin and kanamycin in the treatment of strangulation obstruction. It was believed that another of the broad spectrum antibiotics should be used with penicillin; chloramphenicol was chosen because in its succinate form it causes little local irritation and it can be given in large doses. Feces II (1 cc./kg.) was given to 94 dogs; two hours later the antibiotic combinations were given intraperitoneally. Throughout the studies, in all the succeeding experiments, 0.03 Gm. of kanamycin and 0.03 Gm. of streptomycin per kilogram of body weight were used. This was believed to be comparable to the maximum daily dose used in adults. This dose would mean 2.1 Gm. for a 70 kg. man. Chloramphenicol succinate, 0.1 Gm./kg. was given, which would compare favorably with a large non-

TABLE 3. *Comparison of Antibiotic Combinations on Experimental Peritonitis (Series A)*
Feces II (1 cc./kg.)—2-hour delay then intraperitoneal antibiotic injection

Antibiotic	No. Dogs	No. Surviving	% Survival	P Value
Control	35	8	23	
Penicillin (1 million units) Kanamycin (0.03 Gm./kg.)	20	18	90	
Penicillin (1 million units) Streptomycin (0.03 Gm./kg.)	19	17	89	<0.50
Penicillin (1 million units) Chloramphenicol (0.1 Gm./kg.)	20	15	75	
	94			

toxic dose of 7.0 Gm. for a 70 kg. man.[6] In each animal, irrespective of weight, one large nontoxic dose of 1 million units of penicillin was used.

There was a significant difference between the treated animals and the control group. There was, however, no significant difference noted between any of the combinations used. A 90 per cent survival rate was seen with penicillin-kanamycin and a 75 per cent survival rate with penicillin-chloramphenicol, but the difference between these two was not statistically significant (Table 3).

In an attempt to further determine if there might be any differences between these same antibiotic combinations, a group of 100 animals were challenged with 1.25 cc./kg. of another fecal suspension, Feces III. There was a 20 per cent survival in the control group. Again there was no significant difference between any of the combinations used (Table 4).

From these two series of 194 animals, there is evidence that in this experimental preparation no significant difference exists between the use of penicillin-kanamycin, penicillin-streptomycin and penicillin-chloramphenicol when given intraperitoneally.

Effect of Route of Administration of Antibiotics on Experimental Peritonitis. To evaluate the intravenous, intraperitoneal

TABLE 4. *Comparison of Antibiotic Combinations on Experimental Peritonitis (Series B)*
Feces III (1.25 cc./kg.)—2-hour delay then intraperitoneal antibiotic injection

Antibiotic	No. Dogs	No. Surviving	% Survival	P Value
Control	20	4	20	
Penicillin (1 million units) Kanamycin (0.03 Gm./kg.)	40	28	70	<0 70
Penicillin (1 million units) Streptomycin (0.03 Gm./kg.)	20	16	80	
Penicillin (1 million units) Chloramphenicol (0.1 Gm./kg.)	20	15	75	
	100			

TABLE 5. *Effect of Route of Administration of Antibiotics on Experimental Peritonitis (Immediate)*

Feces III (1.5 cc./kg.)—followed by immediate penicillin (1 million units) and kanamycin (0.03 Gm./kg.)

Route	No. Dogs	No. Surviving	% Survival	P Value
Control	23	0	0	
Intravenous	30	17	57	<0.001
Intraperitoneal	30	17	57	
Intramuscular	30	17	57	
	113			

and intramuscular routes of administration of antibiotics, it was decided to use penicillin and the broad spectrum bactericidal agent, kanamycin. This combination was given in the same dose by each route of administration. Dogs were given a large dose, 1.5 cc./kg. of Feces III. None of the 23 control dogs survived. The drugs were given almost immediately after the challenging dose of the fecal suspension was administered intraperitoneally. All three routes of administration produced the same results; 17 of 30 dogs survived (Table 5),

To further evaluate various routes of administration, an experiment of different design was conducted. A dose of 1.25 cc./kg. of Feces III was injected and the administration of antibiotics delayed for two hours. Of the control dogs 20 per cent survived. In the intravenous group 89 per cent and in the intramuscular group 55 per cent survived, which represents a significant difference between these two groups (Table 6). In the intraperitoneal group 75 per cent survived. This was not significantly different from the survival rate in either the intravenous or the intramuscular groups.

If the antibiotic combination is injected immediately after the fecal suspension is given, the route of administration makes little difference. If peritonitis is allowed to develop with a delay of two hours between injection and the administration of the antibiotic combination, it is evident that the intravenous route of administration is better than the intramuscular route.

Effect of Irrigation on Experimental

TABLE 6. *Effect of Route of Administration of Antibiotics on Experimental Peritonitis (Delayed)*

Feces III (1.25 cc./kg.)—2-hour delay followed by penicillin (1 million units) and kanamycin (0.03 Gm./kg.)

Route	No. Dogs	No. Surviving	% Survival	P Value
Control	20	4	20	
Intravenous	19	17	89	<0.50
Intraperitoneal	20	15	75	<0.05
Intramuscular	20	11	55	
	79			

TABLE 7. *Effect of Immediate Irrigation on Experimental Peritonitis*

Feces III (2.0 cc./kg.)—15-minute delay followed by irrigation plus intraperitoneal penicillin (1 million units) and kanamycin (0.03 Gm./kg.)

	No. Dogs	No. Surviving	% Survival	P Value
Control	20	9	45	<0.025
Irrigation (saline)	20	17	85	
	40			

Peritonitis. To test the value of irrigation of the peritoneal cavity as a method of treatment, a large dose of 2.0 cc./kg. of Feces III was injected into the peritoneal cavity. After a 15-minute delay the dogs were opened, the peritoneal cavity was lavaged with one liter of saline, and antibiotics were administered. Antibiotics were given in addition to irrigation because this is the technic usually employed clinically. The control dogs in this series that received the antibiotics, but no anesthesia or laparotomy, showed a 45 per cent survival rate (Table 7). After irrigation with saline 85 per cent of the anmials survived. This is a significant difference from the control group indicating that early irrigation has a very definite beneficial effect.

In another series of 60 animals the effect of delayed irrigation was tested (Table 8). Dogs were injected with 1.5 cc./kg. of Feces III. After a two-hour delay, irrigation was carried out in one group with 0.25 per cent neomycin solution and in another group with saline. All groups received antibiotics at the end of the irrigation. Of the control animals 60 per cent survived; 80 per cent of the animals irrigated with neomycin and 70 per cent of the animals irrigated with saline survived. There was no significant difference between the irrigated animals and the control group in this experiment.

Changes in Hematocrit in Experimental Peritonitis. Changes in the hematocrit after various treatment regimens are shown in Figure 2. Dogs were injected with 1.25 cc./kg. of Feces III. Some received no treatment, another group received penicillin and kanamycin intraperitoneally, and

TABLE 8. *Effect of Delayed Irrigation on Experimental Peritonitis*

Feces III (1.5 cc./kg.)—2-hour delay followed by irrigation plus intraperitoneal* penicillin (1 million units) and kanamycin (0.03 Gm./kg.)

	No. Dogs	No. Surviving	% Survival	P Value
Control (laparotomy)	20	12	60	<0.30
Irrigation (neomycin 0.25%)	20	16	80	
Irrigation (saline)	20	14	70	
	60			

* Penicillin and kanamycin given I.M. in the neomycin group.

a third group received an infusion of physiologic saline (35 cc./kg.). There was a rapid rise in hematocrit in the nontreated and antibiotic-treated groups in accord with the hemoconcentration that occurs in peritonitis. The rise in the antibiotic-treated group was similar to the rise in the nonantibiotic-treated group. The rise in hematocrit in the saline-treated group was considerably less. This corroborates the time-honored practice of the use of electrolyte solutions in peritonitis. Certainly it is one of the important facets of therapy in clinical patients. Recently in two patients, the use of Dibenzyline in saline has been of value in the treatment of shock following peritonitis. The effect of various fluid regimens and drugs on survival rate in experimental peritonitis is the subject of another report.

Discussion

In most hospitals today peritonitis is treated either by a combination of penicillin and streptomycin or by the use of one of the broad spectrum antibiotics such as oxytetracycline, chlortetracycline, chloramphenicol or kanamycin. From the evidence presented in this report it appears that a combination of penicillin and kanamycin is superior to either antibiotic agent alone. Zintel *et al.*[14] concluded that penicillin therapy alone over a period of ten days was as effective as a combination of penicillin and streptomycin in experimentally produced peritonitis in dogs. Since these studies, however, there has been abundant clinical evidence of the value of a combination of penicillin and streptomycin. Reiss *et al.*,[7] in a study of 68 patients treated with Terramycin, believed this was a good antibiotic agent. Their comment, however, was that the combined use of penicillin-streptomycin had real merit and that Terramycin should be used as an alternate antibiotic when the patient failed to respond to penicillin-streptomycin therapy. Barbieri *et al.*[1] found intravenous

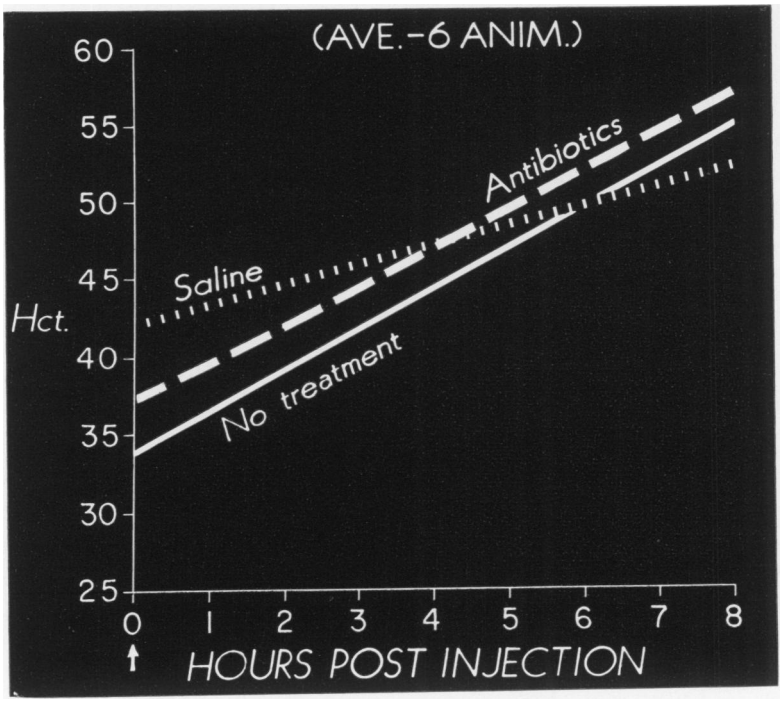

FIG. 2. Graph of hematocrit changes occurring in no treatment, antibiotic-treated and saline-treated dogs after intraperitoneal injection of Feces III, 1.25 cc./kg.

Aureomycin to be an effective agent in the treatment of experimental peritonitis in the dog. During the same studies they pointed out that chloramphenicol in doses of 100 mg./kg. of body weight produced a significant increase in survival times and made a plea for further investigation of this drug. It would seem, however, that irrespective of the broad spectrum antibiotic used it should always be combined with large doses of penicillin.

For many years the value of the intravenous route of administration of antibiotics in the treatment of peritonitis has been emphasized. Schweinburg and associates,[10] by comparing results obtained after intraperitoneal, intramuscular, intravenous and postoperative oral administration of Aureomycin in experimental peritonitis, found that intraperitoneal administration was the most effective method of sterilizing the peritoneal cavity. Silvani *et al.*[11] demonstrated that intraperitoneal administration of streptomycin effectively sterilized the peritoneal cavity of dogs with peritonitis, whereas intramuscular administration did not significantly alter the bacterial flora of the peritoneal exudate. Schatten and Abbott[9] produced experimental appendiceal peritonitis in dogs. When the animals were treated with Terramycin intravenously the mortality rate was 100 per cent. When treated intraperitoneally the mortality rate was 41.1 per cent. This excellent study encouraged the further trial of intraperitoneal antibiotics in peritonitis. Barnett[2] demonstrated the superior value of the intraperitoneal route of administration of antibiotics in strangulation obstruction.

For some time, at the University Hospital, several surgeons have used a combination of intraperitoneal kanamycin and penicillin in the treatment of peritonitis with excellent results. In two poor-risk patients who received curare, intraperitoneal injection of kanamycin during anesthesia was followed by apnea. Thus, the injection of kanamycin into the peritoneal cavity is always delayed until after the patient awakens. The technic currently in vogue is to place a small polyethylene catheter through the abdominal wall into the peritoneal cavity at the time of operation. Kanamycin, 0.5 Gm. in 100 ml. of saline is injected through the catheter three or four times a day during the first 48 hours after operation.

There is some experimental and clinical evidence of the value of antibiotics administered intraperitoneally in the treatment of peritonitis. The studies in this report, however, show in multiple experiments no statistically significant improvement of the intraperitoneal route over the intravenous and intramuscular routes. The intravenous route, however, was significantly better than the intramuscular route in one large series. It would seem that in every instance, when peritonitis is suspected, a combination of antibiotics should be started immediately by the intravenous route. There is little doubt about the value of antibiotic therapy, and the earlier the better. Later, according to the conditions found at operation, it may seem logical to continue intravenous therapy or to administer intraperitoneal antibiotics for two days to be followed by intravenous or intramuscular therapy. Although intravenous kanamycin was given in moderate amounts to many dogs in this study without toxicity, warning is given against the use of this drug intravenously in patients. There is evidence in some preliminary studies that large doses of kanamycin given intravenously in dogs will cause death. When kanamycin is used clinically it should be given by either the intramuscular or intraperitoneal route. If intravenous administration appears mandatory, the manufacturer's recommendations should be followed closely.

Burnett *et al.*[4] presented both clinical

and laboratory evidence that peritoneal lavage with large quantities of saline is a valuable adjunct in the treatment of peritonitis. Barnett and Hardy[3] have demonstrated the value of irrigation of the peritoneal cavity in strangulated intestinal obstruction. Very conclusive evidence is presented in this report of the value of early irrigation of the peritoneal cavity with saline in experimental peritonitis. It would seem reasonable that removing the major portion of the stimulus, namely, large amounts of purulent material and bacteria, from the peritoneal cavity would be beneficial. Undoubtedly, the most important aspect in clinical management of peritonitis is antibiotic therapy and elimination of the focus causing the peritoneal soiling. Lavage of the peritoneal cavity with large quantities of saline, however, would appear from all evidence available today to be of considerable value.

Summary

Various aspects of therapy have been evaluated in a special preparation of experimental peritonitis in dogs. Peritonitis was produced by the injection into the peritoneal cavity of a standarized suspension of dog feces. An evaluation of various modalities of therapy was carried out in 923 animals.

A combination of penicillin and kanamycin produced significantly more survivals than either antibiotic when used alone. There was no significant difference in survivals between the penicillin and the kanamycin treated groups.

Multiple experiments in a significant number of animals showed that penicillin-streptomycin, penicillin-kanamycin and penicillin-chloramphenicol were of considerable value and that there was no significant difference in their efficacy.

The value of routes of administration of penicillin-kanamycin was tested in two experiments of different design. Identical results were obtained by each route of administration when the antibiotic was given immediately after peritoneal contamination. When antibiotic administration was delayed two hours, the intravenous method was significantly better than the intramuscular method. The number of survivals after treatment by the intravenous route was not significantly greater than the number treated by the intraperitoneal route. Similarly, survivals in the group treated intraperitoneally were not significantly different from the number of survivals in the group treated intramuscularly.

Early irrigation of the peritoneal cavity with saline combined with antibiotic therapy gave significantly superior results to antibiotic therapy alone.

Acknowledgments

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Discussion

Dr. Isidore Cohn, Jr. (New Orleans): I am sure all of you are aware of the tremendous amount of work that has gone into the results which Dr. Artz has just presented. I have had the privilege of reading this paper and I would like to make a few comments on the basis of what I have had an opportunity to read.

It is difficult to object to anything that involves as much work as this paper obviously does. Nevertheless, I think there are some things that one would like to see in the paper and one would hope that Dr. Artz and his colleagues would include in any extension of this work that they might do.

At no place have they characterized the feces which they have used as their infecting agent. I believe if either they or others are to repeat this work it would be nice if we knew qualitatively and quantitatively, aerobically and anaerobically, the bacteriologic characteristics of the material they are using as well as any other characteristics they could give us about this particular medium.

In the bacteriologic culture work which they have reported there are no anaerobic studies. Any study of peritonitis, particularly that which is derived from a fecal insult, should have anaerobic cultures so that we can know with what we are dealing.

They are producing peritonitis by a single insult method which, while it has been shown in this work and other work to be a highly lethal disease, is not exactly the kind one would see in a clinical situation where one is more likely to deal with a continuing spill from some source within the abdominal cavity.

Finally, I believe it is unfortunate they have not tried larger doses of some of the antibiotics. In unanesthetized dogs we have found it perfectly safe to place over 1.0 gm./kg. of kanamycin in the peritoneal cavity, and in dogs anesthetized with ether we have had no difficulty in placing over 500 mg./kg. of kanamycin in the peritoneal cavity.

Now that I have made these few minor objections, there are some very valuable points that I think have come out of the work. They have shown quite clearly that it is important to clean out the peritoneal cavity when there is any infection present and the sooner one cleans it out, the better it is.

They have also shown that intraperitoneal antibiotics have a place, and a valuable place, in the treatment of any peritoneal infection. Our own studies of peritonitis have shown that it is very worthwhile to use antibiotics in the peritoneal cavity and we recommend it.

Dr. Albert W. Hartman (San Antonio): I want to bring out a point that I think is important in this paper: the use of such a large number of animals.

I do not know how many of you have had the experience of being the butt of a campaign by the Society for the Prevention of Cruelty to Animals, but you realize that that is always a problem in experimental work.

We had the pleasure of working with Curt in San Antonio at Brooke Army Hospital and I do